Measurement tools of resource use and quality of life in clinical trials for dementia or cognitive impairment interventions: a systematically conducted narrative review

Abstract

Objective: Knowledge is limited about the standardised instruments used to collect resource use and quality of life data alongside trials of dementia interventions. This review aimed to identify the trials using such instruments in order to guide the design of future trial-based cost-effectiveness studies.

Methods: In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement, this review examined all original, peer-reviewed research in major databases and general searches published until June 2017, including randomised clinical trials, pilot studies or feasibility studies about interventions for older adults with dementia or cognitive impairment.

Results: Forty-one studies were identified. Only 8 collected the resource use data using adapted Client Service Receipt Inventory (CSRI), Resource Use Inventory (RUI), cost diary or study-specific questionnaire. Quality of life was assessed using a wide range of instruments. The most frequently used dementia-specific instrument was Quality of Life in Alzheimer's Disease (QOL-AD) and Dementia Quality of Life questionnaire (DEMQOL). Among the generic measures, EuroQol 5-dimentison (EQ-5D) was mostly used to collect health utility data and Short Form surveys (SF-36 or SF-12) were widely to measure general health.

Conclusions: Several useful resource use and quality of life measurement instruments have been identified by this review. For resource use, CSRI was mostly used, but no studies have used Resource Utilisation in Dementia (RUD); for quality of life, we recommend the inclusion of dementia-specific DEMQOL, generic SF-12, and health utility EQ-5D-5L, based on both self- and proxy-report.

Keywords

Resource use, quality of life, instrument, clinical trial, dementia

Introduction

Dementia is a growing public health problem (Scholzel-Dorenbos et al., 2007) and the worldwide cost of dementia has been estimated to exceed those of other chronic diseases (Wimo et al., 2010). Some new treatments have been developed, which could contribute to the care of people with dementia and their families in a wide range of domains (Moniz-Cook et al., 2008a). Given the finite health care budget, economic evaluations aiming to support decision making about these new treatments in dementia are essential. Ideally, these evaluations should be based on long-term clinical trial results that capture the benefits and costs of the intervention (Hughes et al., 2016).

Cost-utility analysis is the most widely used form of economic evaluation. In such analysis, quality-adjusted life year (QALY) is routinely used as the summary measure of health outcomes, which takes both the quantity and quality of life into account. In dementia research, Quality of Life (QoL) has been recognised as an important measure as the clinical measures. Several instruments have specifically been developed to assess QoL in dementia (Scholzel-Dorenbos et al., 2007, Bowling et al., 2015). According to the most recent systematic review (Bowling et al., 2015), more than 10 QoL measures were identified and properties assessed, but this review was limited to disease-specific QoL measures only, and such measures may not be used directly to generate health utility scores for QALYs calculations in cost-utility analysis. With regard to the QoL measures used in clinical trials of dementia, a systematic review done by Schölzel-Dorenbos et al (Scholzel-Dorenbos et al., 2007) found only 3 studies and 2 QoL scales. To our knowledge, this is the only review of this type. Following this review, many new QoL instruments were developed and widely used, including the Dementia Quality of Life questionnaire (DEMQOL) (Smith et al., 2005).

But whether these instruments are appropriate for data collection in clinical trials is still not clear.

Another important component of cost-utility analysis is resource use. According to the Good Research Practices Task Force for cost-effectiveness analysis alongside clinical trials developed by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) (Ramsey et al., 2015), instruments are recommended for cost data collection to improve the quality and uniformity of data generated from trials. But it is not practical to have standardised instruments to measure costs since the range of services to be costed in an economic evaluation depends a lot on the type of intervention and the data sources available. To address this issue, some investigators use questionnaires that could be tailored to meet the needs of each individual study. A frequently used questionnaire is the client service receipt inventory (CSRI) and it has been widely used and adapted to collect data in some observational studies in dementia (McCrone, 2009). Alternatively, there is one standardised and dementia-specific tool available to collect resource use data, Resource Utilisation in Dementia (RUD) instrument (Wimo et al., 2013). It has been used in clinical drug trials and observational studies (Wimo et al., 2003, Wimo and Winblad, 2003). But there is a lack of information about the use of RUD in clinical trials, especially for non-pharmacological interventions, and whether there are other instruments available to collect resource use data in such trials is yet unknown.

Therefore, this review aimed to identify the trials using resource use and QoL measures to collect data in clinical trials about dementia or cognitive interventions and then describe and compare these instruments in terms of their performance in trials, in order to provide a

foundation for the study design of future clinical trial-based cost-utility analysis of dementia or cognitive interventions.

Methods

In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Statement (Moher et al., 2009), this review followed the published protocol (Yang et al., 2017) and consisted of acquiring, extracting and assessing the data (Figure 1).

Eligibility criteria

The eligibility criteria were:

- Population - older adults with dementia or cognitive impairment
- Intervention - all types of interventions, both drug and nondrug therapies
- Comparator - no intervention or the usual care
- Outcomes - measurement and reporting of QoL, or resource use or both
- Study type - randomised clinical trial (RCT), or feasibility study or pilot study

The definition of 'older patients with dementia or cognitive impairment' used in this review was based on each individual study if it described its population as being old adults with dementia or cognitive impairment. Quality of life is an abstract and broad concept including physical function, perceptions of well-being, satisfaction, and sense of self-worth. It has to be assessed by using questionnaires to survey the relevant subjects. Both the profile-based and preference-based QoL instruments were eligible for this review. An instrument is profile-based if it measures different domains of health-related QoL and generates a score for each of these domains, e.g. 36-item Short-Form (SF-36). If an instrument measures the utility of

certain health outcomes, the instrument is preference-based, e.g., the EuroQol 5-dimension (EQ-5D) (Rabin and de Charro, 2001), which could provide a single overall health utility score for QALYs calculation. Given the aim of this review was to guide cost-utility analysis study design, health utility, quality-adjusted life years and QALYs were also used as the search terms. We included RCT or pilot/feasibility studies using RCT design, which were small-scale preliminary studies conducted prior to the full RCTs in order to evaluate feasibility, effects, etc.

Search strategy

The following major databases (Ovid Medline, PsycINFO, EMBASE, CINAHL, Cochrane Databases of Systematic Reviews, Web of Science and Scopus) were searched in September 2016 and the searches were re-run before the final analyses in June 2017. A hand search of the references of included articles and general search, e.g. Google Scholar, were also conducted to identify potential relevant studies. Key terms were determined through discussion between authors. The search strategies were created specifically for each database using relevant index and free text terms (see Appendix 1 for the terms used in Ovid Medline). Studies were eligible regardless of the language or date of publication, but the abstract was available in English.

Article selection

All results were exported into Endnote X7 software (Thomson Reuters, 2016). After dropping duplicates, all the titles and abstracts of the studies retrieved were imported to an Excel spreadsheet (Microsoft Corporation, 2010). The first author (F.Y.) screened all the abstracts to rule out the literature reviews, meta-analyses, clinical guidelines, study protocols, editorials, letters, commentaries, case reports, and conference proceedings that were not

recognised as original articles. Two authors (F.Y. and B.G.) independently screened the titles and abstracts of the remaining articles against the inclusion criteria. If a title or abstract suggested that the trial was eligible, or if there was insufficient information to make a decision, the full-text was retrieved and assessed for eligibility independently by both authors. Discrepancies were resolved through discussion or adjudication by a third author (P.D.) if necessary.

Data extraction

We developed a standardised excel sheet to extract data from the included studies, including publication characteristics, participant characteristics, intervention characteristics, and instrument characteristics.

Data synthesis

First, the characteristics of included studies were tabulated. Second, we summarised the frequency of each instrument used in the trials. Third, the characteristics of each QoL instrument were described and tabulated, using a table adapted from the one used in a review of dementia-specific QoL scales (Bowling et al., 2015), including instrument, conceptual basis, patient/proxy report, patient population, subscales, items, response options and scoring.

Results

Search results

The searches yielded 2527 records. After removing duplicates, the title and abstract of 1089 unique records were screened. 65 were sought for full-text screening and 41 studies were eligible for inclusion.

Study characteristics

The studies were published between 2000 and 2017 and conducted in 15 countries/regions, most frequently in the US, the UK and Australia (Table 1). Most of studies were RCTs (73.2%) and nearly half of the studies included both dementia and mild cognitive impairment patients (46.3%). Majority studies aimed to assess the non-pharmacological interventions (85.4%).

Resource use measure

Among the 41 studies included, 8 studies collected resource use data. Healthcare costs were calculated by multiplying the number of units of each type of service received by the unit cost of that service estimated from published reports and administrative datasets and summing the products across different services. Resource use data were collected using multiple instruments, including Client Service Receipt Inventory (CSRI), Resource Use Inventory (RUI), cost diary and informal care survey, and a study-specific questionnaire developed specifically for that study.

Client Service Receipt Inventory (CSRI)

There were 5 studies using adapted CSRI to collect resource use data (Knapp et al., 2006, Woods et al., 2012, Banerjee et al., 2011, Romeo et al., 2013, D'Amico et al., 2015, Knapp et al., 2016, Howard et al., 2012). All studies were conducted in the UK, ranging from mild to severe dementia. The CSRI was developed by Knapp and Beecham in the mid-1980s to collect detailed information on healthcare services received, medication, and wider carer economic impacts. It has five sections: background client information; accommodation and living situation; employment history, earnings and benefits; a record of services and unpaid cares (PSSRU). One of the CSRI's greatest strengths is its adaptability. A large number of

versions of it have been produced to suit the needs of each individual study, and it has been extensively used in studies of mental health and dementia. The CSRI is usually completed through interviews with patients and their caregivers.

Resource Use Inventory (RUI)

In the Finnish study for people with mild cognitive impairment (Kivipelto et al., 2013), utilisation of health resources were estimated using register data and questionnaire data. The questionnaire used in this study was the Resource Use Inventory (RUI) (Sano et al., 2006), which was developed to capture resource utilisation and costs in populations with Alzheimer's disease. The RUI was completed by the patient and the carer together. It consisted of 9 questions to document the use of direct medical services and nonmedical care. The RUI also includes questions to capture the time caregivers spend providing care to the patients and the time use of the patients by participating in paid and volunteer work.

Cost diary and survey

In a study for Dutch dementia patients (Wolfs et al., 2009), resource use data were estimated using the hospital and pharmacy datasets, the informal care surveys, and cost diaries. The informal care survey was developed by van den Berg et al for the measurement and valuation of informal care (van den Berg et al., 2005). In this survey, informal caregivers were asked to indicate the average time spent on different informal care tasks per week, at baseline and at follow-ups. The carers were also asked to complete the cost diaries at both baseline and follow-ups to determine the costs made outside the hospital that could not be gathered from the hospital or pharmacist's registrations. Cost diaries are an accepted method to assess resource use in cost-effectiveness studies (Goossens et al., 2000).

Study-specific questionnaire

In the cost-benefit analysis of drug therapies for outpatients with Alzheimer's disease done in US (Rosenheck et al., 2007), a questionnaire was developed for this study and was completed by the caregiver every month to document the healthcare service use, including hospital stays, outpatient services, community supports and other related services.

QoL measure

The quality of life was assessed using a wide range of instruments across the studies (Table 2). We noted 15 different QoL instruments, with 5 dementia-specific and 10 generic. Multiple measures were used in several studies.

Dementia-specific measure

The dementia-specific instruments identified were: Quality of Life in Alzheimer's Disease (QOL-AD) (n=22), Dementia Quality of Life questionnaire (DEMQOL) (n=4), Quality of Life in Late-stage Dementia (QUALID) (n=3), Alzheimer's Disease Related Quality of Life (ADRQL) (n=2), and Dementia Quality of Life Instrument (DQOL) (n=1). The characteristics of these instruments were summarised in Table 3.

Quality of Life in Alzheimer's Disease (QOL-AD)

QOL-AD was designed to measure the quality of life among individuals living with Alzheimer's disease (Logsdon et al., 1999). It includes both self-rating version with 13 items and proxy-rating (by family carer or staff) version with 15 items. The items ask the patient/proxy to score aspects of physical health, energy level, mood, living situation, memory, family, marriage, friends, self, ability to do chores and things for fun, money, and life as a whole using 4-point scales (poor/fair/good/excellent). Both the patient and proxy

versions have been used in the identified studies. QOL-AD score ranges from 13 to 52 for patient version and 15 to 60 for proxy version, with higher scores representing better quality of life. It is recommended by the European consensus on outcome measures for psychosocial interventions in dementia (Moniz-Cook et al., 2008b).

Dementia Quality of Life questionnaire (DEMQOL)

The DEMQOL is a 28-item instrument, which covers five domains of quality of life (daily activities and looking after self; health and well-being; cognitive functioning; social relationships; self-concept), aiming to assess QoL in people with mild to moderate dementia (Smith et al., 2005). A proxy version was developed for caregivers, DEMQOL-Proxy, with 31 items. A 4-point Likert scale (a lot/quite a bit/a little/not at all) is used to collect responses to each item. A Likert scale measures attitudes and behaviours using answer choices that range from one extreme to another and thus allows the respondent to uncover degrees of opinion. In the eligible studies, DEMQOL and DEMQOL-Proxy were used together with the exception of DEMQOL-Proxy for people with moderate to severe dementia (Knapp et al., 2016). Score ranges from 28 to 112 for DEMQOL and 31 to 124 for DEMQOL-Proxy. Higher scores indicate better QoL. In addition, health utility values can be generated from DEMQOL (DEMQOL-U) and DEMQOL-Proxy (DEMQOL-Proxy-U) to enable the QALYs calculation for cost-utility analysis (Mulhern et al., 2013). This approach has been used in the economic evaluation study of a maintenance cognitive stimulation therapy for people with mild-to-moderate dementia in the UK (D'Amico et al., 2015).

Quality of Life in Late-stage Dementia (QUALID)

QUALID was designed specifically for use with people with late-stage dementia in institutional settings and it measures 11 observable behaviours including both positive and

negative dimensions of observable activity and emotional states. The assessments are based on concrete observable behaviours, so it is usually completed by nursing staff. Items are rated on a 5-point Likert scale which captures the frequency of each item and score ranges from 11 to 55 with lower scores representing better QoL. The QUALID has been recommended by the Swedish Dementia Centre to estimate QoL in dementia patients (Nordgren and Engstroem, 2014).

Alzheimer's Disease Related Quality of Life (ADRQL)

ADRQL was developed for patients with Alzheimer's disease to assess multidimensional domains of QoL in dementia that patients, caregivers, and experts identified as important (Rabins et al., 1999). It has 48 items, grouped into 5 domains, measuring the observable behaviours and actions. It is used for family caregivers' proxy ratings of the patient's QoL. A 4-point Likert scale is used in ADRQL (not at all/not very/somewhat/very much) and scores are calculated using a preference-based weighting approach, which means that weights for QoL indicators vary according to the importance of the domain. Higher scores reflect better quality of life.

Dementia Quality of Life Instrument (DQOL)

DQOL contains 30 items, forming 5 subscales related to QoL: aesthetics, positive affect, absence of negative affect, belonging, and self-esteem (Brod et al., 1999). It was developed through literature review and consultation with expert panels composed of dementia patients, caregivers, and professional care providers (Ready and Ott, 2003). Items are rated on one of two 5-point Likert scales (ranging from not at all to a lot, and never to very often) and DQOL yields scores on 5 subscales. Lower scores on 'negative affect' and higher scores on other subscales indicate worse QoL.

Generic QoL measure

Among the 10 generic QoL measures, 3 health utility measures were included: EQ-5D (n=5), 15-dimension (n=1) and Health Utilities Index Mark 3 (HUI3) (n=1). Other generic instruments were: 36-item Short-Form (SF-36) (n=2), 12-item Short-Form (SF-12) (n=1), 12-item General Health Questionnaire (GHQ-12) (n=1), 15-item Quality of Life Scales (QOLS) (n=1), Anamnestic Comparative Self-Assessment Scale (ACSA) (n=1), QOL Face Scale scores (n=1), and Quality of Life Assessment-Patient (QLA-P) (n=1).

EuroQol 5-dimension (EQ-5D)

The EQ-5D is a generic, utility-based QoL instrument. It can be simply administered to patients in the form of a self-completed questionnaire. All the identified studies used the 3-level version (EQ-5D-3L), which consists of 5 domains (mobility, self-care, usual activities, pain and discomfort, and anxiety and depression) and 3 levels for each domain (no problems/some problems/extreme problems or unable). According to the domains and levels, EQ-5D-3L yields 243 potential health states, each of which is assigned a utility weight, range from -0.594 to 1 using a utility scoring function derived from the UK general population. High scores represent higher utility. Among the 5 studies using EQ-5D as an outcome measure, 3 studies included both self-rated and proxy-rated EQ-5D (Romeo et al., 2013, D'Amico et al., 2015, Hoffmann et al., 2016). The EQ-5D is recommended by the National Institution for Health and Care Excellence (NICE) in England to be used in economic evaluations of health-care interventions (NICE, 2013).

15-dimension (15D)

15D is a generic health utility QoL measure (Sintonen, 2001). It consists of 15 dimensions (mobility, vision, hearing, breathing, sleeping, eating, speech, excretion, usual activities,

mental function, discomfort and symptoms, depression, distress, vitality, and sexual activity) with 5 ordinal levels. Similar to EQ-5D, a single index score measure can be calculated from the health state descriptive system by using a set of utility weights. The index score ranges from 0 to 1 (Sintonen, 2001). The 15D scores have been shown to be reliable, sensitive and responsive to change, and valid for deriving QALYs (Sintonen, 2001). In the identified study (Kivipelto et al., 2013), it was measured directly from the participants, who were at risk of cognitive decline.

Health Utilities Index Mark 3 (HUI3)

HUI3 is also a generic health utility measure consisting of eight attributes: hearing, vision, speech, ambulation, dexterity, emotion, cognition, and pain. Each attribute has multiple functioning levels. To calculate the HUI3 score, a utility scoring function derived from a representative sample of the Canadian general population is used. Score ranges from -0.36 to 1 with higher scores reflecting better health (Wee et al., 2007). In the study about dementia interventions (Rosenheck et al., 2007), HUI3 was administered to caregivers to rate patients' QoL, supplemented by several disease-specific measures (Rosenheck et al., 2007).

Short Form Surveys (SF-36 and SF-12)

SF-36 is the most widely used profile-based QoL measure, which includes eight areas: physical functioning, role functioning, bodily pain, general health, vitality, social functioning, role-emotional functioning, and mental health. Two summary scores, physical component summary (PCS) and mental component summary (MCS), can be calculated to indicate the patients' QoL, ranging from 0 to 100 with higher scores representing better health. SF-12 is the abridged version of SF-36, and it has been used increasingly because of its lower burden to respondents and similar measurement properties as its longer version (Ware et al., 1996).

In the trials identified (Kivipelto et al., 2013, Gates et al., 2014, Kwok et al., 2013), both instruments were used to collect data from patients with mild cognitive impairment directly at baseline and follow-ups.

12-item General Health Questionnaire (GHQ-12)

GHQ-12 measures two main areas with 12 items: the inability to carry out normal functions and the appearance of new and distressing phenomena. In the study identified from this review (Graff et al., 2007) , GHQ-12 was used to ask patient to rate their own QoL. The score ranges from 0 to 36 with lower scores indicating better health.

15-item Quality of Life Scales (QOLS)

QOLS has 15 items that measures five domains of life: material and physical well-being; relationships with other people; social, community, and civic activities; personal development and fulfilment; and recreation (Burckhardt and Anderson, 2003). The QOLS scores range from 16 to 112 with higher scores indicating better quality of life (Burckhardt and Anderson, 2003). It was used to collect data from individuals with mild cognitive impairment directly (Gates et al., 2014).

Anamnestic Comparative Self-Assessment Scale (ACSA)

ACSA is a ten-stage anchor scale for a global assessment of present quality of life defined in terms of the 'best time' versus the 'worst time' in life. A higher quality of life is reflected by an improvement in the global scale score. It was completed by the patients themselves at both baseline and follow-up (Walter et al., 2007).

QOL Face Scale

QOL Face Scale is a 9-choice picture format with a score range of 1-9 (worst=1, best=9, from frowning to smiling faces) assessing the degree of general happiness in current daily life. It was used to ask the caregivers to answer these questions on behalf of the patients with dementia (Nakatsuka et al., 2015).

Quality of Life Assessment-Patient (QLA-P)

QLA-P is a rating scale completed by caregivers to assess broad areas of patient's quality of life. The original version includes 10 categories (working, leisure, eating, sleeping, social contact, earning, parenting, loving, environment, and self-acceptance). In the identified study (Davis et al., 2001), the scale was adapted to increase its relevance to patients with Alzheimer's disease. Each category is rated using an anchor points (0 and 50), with higher scores reflecting higher QoL.

Discussion

In view of the need for economic assessment of dementia interventions, collecting information on resource use and quality of life using the standardised instruments in clinical trials is important to ensure high quality data for further cost-effectiveness analysis. In this review, we examined 41 studies to identify such instruments used in dementia.

The resource use instruments were seldom used in previous published RCTs or feasibility studies. CSRI and RUI were identified in this review, but the dementia-specific resource use instrument, RUD, was not included. Wimo et al (Wimo et al., 2013) have done a head-to-head comparison of RUD with other resource use instruments, including CSRI and RUI, and

concluded that informal care is the key resource of the RUD instrument and is probably the only item that will not be available from other sources. The inclusion of informal care in RUD could make better estimates of the resource used. Also, RUD is suitable for multinational study as the same resource items should be used across different translations to enable comparison of costs of care across countries. A short version of RUD, RUD Lite (Wimo et al., 2013), is available and it is more appropriate if the caregiver resource use is not central to the study.

For QoL measurement, 5 dementia-specific instruments were identified. These instruments differ in many aspects including conceptual basis, applicability and psychometric properties. QOL-AD measures a broader range of QoL validated during focus groups with patients and carers while DEMQOL focuses on the health-related QoL, which relates only to areas of QoL affected by a health condition. Both instruments have been shown to have good psychometric properties for individuals with mild to moderate dementia (Logsdon et al., 2002, Smith et al., 2005). QUALID was designed for people with late-stage dementia in institutional settings, so it may have limited applicability to those with mild to moderate dementia. ADRQL was developed based on the assumption that the caregivers are best to assess the patients' QoL (Rabins et al., 1999), which has been considered invalid in the case of mild to moderate dementia (Trigg et al., 2007). DQOL is the scale developed exclusively to be administered to patients (Ready et al., 2004) and assesses feeling states and mood, which may fail to capture other QoL areas impact by the disease. Based on the conceptual framework and applicability, QOL-AD and DEMQOL are preferred in future trials of people with mild to moderate dementia, but if the study focuses more about health-related QoL, DEMQOL may be a better choice. Furthermore, as described previously, health utility scores, DEMQOL-Utility, can be generated from DEMQOL, which could be used to complement the generic utility instrument

in future cost-utility analysis (Mulhern et al., 2013), although its validity and responsiveness need further testing.

Regarding the generic QoL measure, we identified 3 instruments that generate health utility scores and 7 other measures. EQ-5D is the most used health utility instrument, but it has been commented to lack sensitivity, especially in the area of mental health (Shah, 2016). Therefore, the 5-level EQ-5D (EQ-5D-5L) is suggested to be used because of its improved sensitivity and reduced ceiling effect. SF-36 and SF-12 are the mostly used generic QoL instruments, providing summary scores of health-related QoL and thus enabling comparisons across different diseases, population groups, and interventions (Patrick and Deyo, 1989). Although SF-36/SF-12 is increasingly used in patients undergoing routine operations, it may fail to observe the small but clinical important differences or changes in dementia study, which could be captured by disease-specific measures. Preferences for generic or disease-specific measures usually depends on the purpose of the study (Patrick and Deyo, 1989); therefore, if a study aims not only to measure the QoL concepts covered by a generic measure, but also to capture the specific concerns related to dementia or cognitive impairment, we suggest to include both generic and dementia-specific measures in the same study.

It should be noted that in previous trials in mild to moderate dementia (D'Amico et al., 2015, Banerjee et al., 2011), both DEMQOL and DEMQOL-Proxy were included. Self-rated and proxy-rated EQ-5D were also used together in several studies (Romeo et al., 2013, D'Amico et al., 2015, Hoffmann et al., 2016). Given the complexity of dementia, researchers suggest that both patient-reported outcomes and observable behaviour, which is based on proxy-reporting, should be included in order to better measure the effects of interventions (Mulhern

et al., 2013). DEMQOL-Proxy has been shown to give complementary perspectives on QoL to DEMQOL (Smith et al., 2005) and thus the use of both measures together is recommend. What's more, at some point patients may be unable to meaningfully assess their own QoL, and under such circumstances, researchers have to rely on other sources such as proxy-reporting. Proxy EQ-5D appears to be an acceptable source of data for QALYs (Devine et al., 2014) and has been used in some studies. But due to the poor agreement between proxy scores and self-reported scores, they cannot be assumed to substitute for each other (Arons et al., 2013) and cost-effectiveness analyses using both approaches should be conducted.

The limitation of this review should be mentioned. Since no quality assessment tool was available for this kind of review and the psychometric properties were not formally compared in this review, our approach necessarily involved subjective judgement.

Conclusions

There is a lack of firm evidence about the use of standardised instrument to collect resource use and QoL data in trials about interventions for dementia. Several useful resource use and quality of life measurement instruments have been identified by this review, which would contribute to the study design of future economic evaluation alongside clinical trials in dementia care. For resource use, CSRI was mostly used, but no studies have used RUD; for QoL, we recommend the inclusion of dementia-specific DEMQOL, generic SF-12, and health utility EQ-5D-5L, based on both self- and proxy-report.

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Conflict of Interest

None to declare.

References

ARONS, A. M., KRABBE, P. F., SCHOLZEL-DORENBOS, C. J., VAN DER WILT, G. J. & RIKKERT, M. G. 2013. Quality of life in dementia: a study on proxy bias. *BMC Med Res Methodol,* 13**,** 110.

BANERJEE, S., HELLIER, J., DEWEY, M., ROMEO, R., BALLARD, C., BALDWIN, R., BENTHAM, P., FOX, C., HOLMES, C., KATONA, C., KNAPP, M., LAWTON, C., LINDESAY, J., LIVINGSTON, G., MCCRAE, N., MONIZ-COOK, E., MURRAY, J., NUROCK, S., ORRELL, M., O'BRIEN, J., POPPE, M., THOMAS, A., WALWYN, R., WILSON, K. & BURNS, A. 2011. Sertraline or mirtazapine for depression in dementia (HTA-SADD): a randomised, multicentre, double-blind, placebo-controlled trial. *Lancet,* 378**,** 403-11.

BOWLING, A., ROWE, G., ADAMS, S., SANDS, P., SAMSI, K., CRANE, M., JOLY, L. & MANTHORPE, J. 2015. Quality of life in dementia: a systematically conducted narrative review of dementia-specific measurement scales. *Aging Ment Health,* 19**,** 13-31.

BROD, M., STEWART, A. L., SANDS, L. & WALTON, P. 1999. Conceptualization and measurement of quality of life in dementia: the dementia quality of life instrument (DQoL). *Gerontologist,* 39**,** 25-35.

BURCKHARDT, C. S. & ANDERSON, K. L. 2003. The Quality of Life Scale (QOLS): reliability, validity, and utilization. *Health Qual Life Outcomes,* 1**,** 60.

D'AMICO, F., REHILL, A., KNAPP, M., AGUIRRE, E., DONOVAN, H., HOARE, Z., HOE, J., RUSSELL, I., SPECTOR, A., STREATER, A., WHITAKER, C., WOODS, R. T. & ORRELL, M. 2015. Maintenance cognitive stimulation therapy: an economic evaluation within a randomized controlled trial. *J Am Med Dir Assoc,* 16**,** 63-70.

DAVIS, R. N., MASSMAN, P. J. & DOODY, R. S. 2001. Cognitive intervention in Alzheimer disease: a randomized placebo-controlled study. *Alzheimer disease and associated disorders,* 15**,** 1-9.

DEVINE, A., TAYLOR, S. J. C., SPENCER, A., DIAZ-ORDAZ, K., ELDRIDGE, S. & UNDERWOOD, M. 2014. The agreement between proxy and self-completed EQ-5D for care home residents was better for index scores than individual domains. *Journal of Clinical Epidemiology,* 67**,** 1035-1043.

GATES, N., VALENZUELA, M., SACHDEV, P. S. & SINGH, M. A. F. 2014. Psychological well-being in individuals with mild cognitive impairment. *Clinical interventions in aging,* 9**,** 779-92.

GOOSSENS, M. E., RUTTEN-VAN MOLKEN, M. P., VLAEYEN, J. W. & VAN DER LINDEN, S. M. 2000. The cost diary: a method to measure direct and indirect costs in cost-effectiveness research. *J Clin Epidemiol,* 53**,** 688-95.

GRAFF, M. J., VERNOOIJ-DASSEN, M. J., THIJSSEN, M., DEKKER, J., HOEFNAGELS, W. H. & OLDERIKKERT, M. G. 2007. Effects of community occupational therapy on quality of life, mood, and health status in dementia patients and their caregivers: a randomized controlled trial. *Journals of Gerontology Series A: Biological Sciences & Medical Sciences,* 62A**,** 1002-1009 8p.

HOFFMANN, K., SOBOL, N. A., FREDERIKSEN, K. S., BEYER, N., VOGEL, A., VESTERGAARD, K., BRAENDGAARD, H., GOTTRUP, H., LOLK, A., WERMUTH, L., JACOBSEN, S., LAUGESEN, L. P., GERGELYFFY, R. G., HOGH, P., BJERREGAARD, E., ANDERSEN, B. B., SIERSMA, V., JOHANNSEN, P., COTMAN, C. W., WALDEMAR, G. & HASSELBALCH, S. G. 2016. Moderate-to-High Intensity Physical Exercise in Patients with Alzheimer's Disease: A Randomized Controlled Trial. *Journal of Alzheimers Disease,* 50**,** 443-453.

HOWARD, R., MCSHANE, R., LINDESAY, J., RITCHIE, C., BALDWIN, A., BARBER, R., BURNS, A., DENING, T., FINDLAY, D., HOLMES, C., HUGHES, A., JACOBY, R., JONES, R., JONES, R., MCKEITH, I., MACHAROUTHU, A., O'BRIEN, J., PASSMORE, P., SHEEHAN, B., JUSZCZAK, E., KATONA, C., HILLS, R., KNAPP, M., BALLARD, C., BROWN, R., BANERJEE, S., ONIONS, C., GRIFFIN, M., ADAMS, J., GRAY, R., JOHNSON, T., BENTHAM, P. & PHILLIPS, P. 2012. Donepezil and Memantine for Moderate-to-Severe Alzheimer's Disease. *New England Journal of Medicine,* 366**,** 893-903.

HUGHES, D., CHARLES, J., DAWOUD, D., EDWARDS, R. T., HOLMES, E., JONES, C., PARHAM, P., PLUMPTON, C., RIDYARD, C., LLOYD-WILLIAMS, H., WOOD, E. & YEO, S. T. 2016. Conducting Economic Evaluations Alongside Randomised Trials: Current Methodological Issues and Novel Approaches. *Pharmacoeconomics,* 34**,** 447-61.

KIVIPELTO, M., SOLOMON, A., AHTILUOTO, S., NGANDU, T., LEHTISALO, J., ANTIKAINEN, R., BACKMAN, L., HANNINEN, T., JULA, A., LAATIKAINEN, T., LINDSTROM, J., MANGIALASCHE, F., NISSINEN, A., PAAJANEN, T., PAJALA, S., PELTONEN, M., RAURAMAA, R., STIGSDOTTER-NEELY, A., STRANDBERG, T., TUOMILEHTO, J. & SOININEN, H. 2013. The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER): Study design and progress. *Alzheimers & Dementia,* 9**,** 657-665.

KNAPP, M., KING, D., ROMEO, R., ADAMS, J., BALDWIN, A., BALLARD, C., BANERJEE, S., BARBER, R., BENTHAM, P., BROWN, R. G., BURNS, A., DENING, T., FINDLAY, D., HOLMES, C., JOHNSON, T., JONES, R., KATONA, C., LINDESAY, J., MACHAROUTHU, A., MCKEITH, I., MCSHANE, R., O'BRIEN, J. T., PHILLIPS, P. P., SHEEHAN, B. & HOWARD, R. 2016. Cost-effectiveness of donepezil and memantine in moderate to severe Alzheimer's disease (the DOMINO-AD trial). *Int J Geriatr Psychiatry*.

KNAPP, M., THORGRIMSEN, L., PATEL, A., SPECTOR, A., HALLAM, A., WOODS, B. & ORRELL, M. 2006. Cognitive stimulation therapy for people with dementia: cost-effectiveness analysis. *British Journal of Psychiatry,* 188**,** 574-580.

KWOK, T., WONG, A., CHAN, G., SHIU, Y. Y., LAM, K.-C., YOUNG, D., HO, D. W. H. & HO, F. 2013. Effectiveness of cognitive training for Chinese elderly in Hong Kong. *Clinical interventions in aging,* 8**,** 213-9.

LOGSDON, R. G., GIBBONS, L. E., MCCURRY, S. M. & TERI, L. 1999. Quality of life in Alzheimer's disease: Patient and caregiver reports. *Journal of Mental Health and Aging,* 5**,** 21-32.

LOGSDON, R. G., GIBBONS, L. E., MCCURRY, S. M. & TERI, L. 2002. Assessing quality of life in older adults with cognitive impairment. *Psychosom Med,* 64**,** 510-9.

MCCRONE, P. 2009. Capturing the costs of end-of-life care: comparisons of multiple sclerosis, Parkinson's disease, and dementia. *J Pain Symptom Manage,* 38**,** 62-7.

MOHER, D., LIBERATI, A., TETZLAFF, J., ALTMAN, D. G. & GROUP, P. 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med,* 6**,** e1000097.

MONIZ-COOK, E., VERNOOIJ-DASSEN, M., WOODS, R., VERHEY, F., CHATTAT, R., DE VUGT, M., MOUNTAIN, G., O'CONNELL, M., HARRISON, J., VASSE, E., DROES, R.

M., ORRELL, M. & GROUP, I. 2008a. A European consensus on outcome measures for psychosocial intervention research in dementia care. *Aging & mental health,* 12**,** 14-29.
MONIZ-COOK, E., VERNOOIJ-DASSEN, M., WOODS, R., VERHEY, F., CHATTAT, R., DE VUGT, M., MOUNTAIN, G., O'CONNELL, M., HARRISON, J., VASSE, E., DROES, R. M., ORRELL, M. & GROUP, I. 2008b. A European consensus on outcome measures for psychosocial intervention research in dementia care. *Aging Ment Health,* 12**,** 14-29.
MULHERN, B., ROWEN, D., BRAZIER, J., SMITH, S., ROMEO, R., TAIT, R., WATCHURST, C., CHUA, K. C., LOFTUS, V., YOUNG, T., LAMPING, D., KNAPP, M., HOWARD, R. & BANERJEE, S. 2013. Development of DEMQOL-U and DEMQOL-PROXY-U: generation of preference-based indices from DEMQOL and DEMQOL-PROXY for use in economic evaluation. *Health Technol Assess,* 17**,** v-xv, 1-140.
NAKATSUKA, M., NAKAMURA, K., HAMANOSONO, R., TAKAHASHI, Y., KASAI, M., SATO, Y., SUTO, T., NAGATOMI, R. & MEGURO, K. 2015. A Cluster Randomized Controlled Trial of Nonpharmacological Interventions for Old-Old Subjects with a Clinical Dementia Rating of 0.5: The Kurihara Project. *Dementia and Geriatric Cognitive Disorders Extra,* 5**,** 221-232.
NICE. 2013. National Institute for Health and Care Excellence: Guide to the methods of technology appraisal 2013. Available: https://www.nice.org.uk/process/pmg9/chapter/evidence [Accessed April 2013].
NORDGREN, L. & ENGSTROEM, G. 2014. Animal-Assisted Intervention in Dementia: Effects on Quality of Life. *Clinical Nursing Research,* 23**,** 7-19.
PATRICK, D. L. & DEYO, R. A. 1989. Generic and disease-specific measures in assessing health status and quality of life. *Med Care,* 27**,** S217-32.
PSSRU. *http://www.pssru.ac.uk/blogs/csri/what-is-the-csri/* [Online].
RABIN, R. & DE CHARRO, F. 2001. EQ-5D: a measure of health status from the EuroQol Group. *Annals of Medicine,* 33**,** 337-343.
RABINS, P. V., KASPER, J. D., KLEINMAN, L., BLACK, B. S. & PATRICK, D. L. 1999. Concepts and methods in the development of the ADRQL: An instrument for assessing health-related quality of life in persons with Alzheimer's disease. *Journal of Mental Health and Aging,* 5**,** 33-48.
RAMSEY, S. D., WILLKE, R. J., GLICK, H., REED, S. D., AUGUSTOVSKI, F., JONSSON, B., BRIGGS, A. & SULLIVAN, S. D. 2015. Cost-effectiveness analysis alongside clinical trials II-An ISPOR Good Research Practices Task Force report. *Value Health,* 18**,** 161-72.
READY, R. E. & OTT, B. R. 2003. Quality of Life measures for dementia. *Health Qual Life Outcomes,* 1**,** 11.
READY, R. E., OTT, B. R. & GRACE, J. 2004. Patient versus informant perspectives of Quality of Life in Mild Cognitive Impairment and Alzheimer's disease. *Int J Geriatr Psychiatry,* 19**,** 256-65.
ROMEO, R., KNAPP, M., HELLIER, J., DEWEY, M., BALLARD, C., BALDWIN, R., BENTHAM, P., BURNS, A., FOX, C., HOLMES, C., KATONA, C., LAWTON, C., LINDESAY, J., LIVINGSTON, G., MCCRAE, N., MONIZ-COOK, E., MURRAY, J., NUROCK, S., O'BRIEN, J., POPPE, M., THOMAS, A., WALWYN, R., WILSON, K. & BANERJEE, S. 2013. Cost-effectiveness analyses for mirtazapine and sertraline in dementia: randomised controlled trial. *Br J Psychiatry,* 202**,** 121-8.
ROSENHECK, R. A., LESLIE, D. L., SINDELAR, J. L., MILLER, E. A., TARIOT, P. N., DAGERMAN, K. S., DAVIS, S. M., LEBOWITZ, B. D., RABINS, P., HSIAO, J. K., LIEBERMAN, J. A., SCHNEIDER, L. S. & INVETIGATORS, C. A. 2007. Cost-benefit analysis of second-generation antipsychotics and placebo in a randomized trial of the treatment of psychosis and aggression in Alzheimer disease. *Archives of General Psychiatry,* 64**,** 1259-1268.
SANO, M., ZHU, C. W., WHITEHOUSE, P. J., EDLAND, S., JIN, S., ERNSTROM, K., THOMAS, R. G., THAL, L. J., FERRIS, S. H. & ALZHEIMER DISEASE COOPERATIVE STUDY, G. 2006. ADCS Prevention Instrument Project: pharmacoeconomics: assessing health-related resource use among healthy elderly. *Alzheimer Dis Assoc Disord,* 20**,** S191-202.

SCHOLZEL-DORENBOS, C. J., VAN DER STEEN, M. J., ENGELS, L. K. & OLDE RIKKERT, M. G. 2007. Assessment of quality of life as outcome in dementia and MCI intervention trials: a systematic review. *Alzheimer Dis Assoc Disord,* 21**,** 172-8.

SHAH, K., MULHERN, B., LONGWORTH, L. AND JANSEN, M.F. 2016. Important aspects of health not captured by eq-5d: views of the UK general public. *EuroQol Working Paper 16001. Rotterdam: EuroQol Research Foundation.*

SINTONEN, H. 2001. The 15D instrument of health-related quality of life: properties and applications. *Ann Med,* 33**,** 328-36.

SMITH, S. C., LAMPING, D. L., BANERJEE, S., HARWOOD, R., FOLEY, B., SMITH, P., COOK, J. C., MURRAY, J., PRINCE, M., LEVIN, E., MANN, A. & KNAPP, M. 2005. Measurement of health-related quality of life for people with dementia: development of a new instrument (DEMQOL) and an evaluation of current methodology. *Health Technology Assessment,* 9**,** 1-+.

TRIGG, R., JONES, R. W. & SKEVINGTON, S. M. 2007. Can people with mild to moderate dementia provide reliable answers about their quality of life? *Age Ageing,* 36**,** 663-9.

VAN DEN BERG, B., AL, M., BROUWER, W., VAN EXEL, J. & KOOPMANSCHAP, M. 2005. Economic valuation of informal care: the conjoint measurement method applied to informal caregiving. *Soc Sci Med,* 61**,** 1342-55.

WALTER, M., HÄNNI, B., HAUG, M., AMRHEIN, I., KREBS-ROUBICEK, E., MÜLLER-SPAHN, F. & SAVASKAN, E. 2007. Humour therapy in patients with late-life depression or Alzheimer's disease: a pilot study. *International Journal of Geriatric Psychiatry,* 22**,** 77-83 7p.

WARE, J., JR., KOSINSKI, M. & KELLER, S. D. 1996. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care,* 34**,** 220-33.

WEE, H. L., MACHIN, D., LOKE, W. C., LI, S. C., CHEUNG, Y. B., LUO, N., FEENY, D., FONG, K. Y. & THUMBOO, J. 2007. Assessing differences in utility scores: a comparison of four widely used preference-based instruments. *Value Health,* 10**,** 256-65.

WIMO, A., GUSTAVSSON, A., JONSSON, L., WINBLAD, B., HSU, M. A. & GANNON, B. 2013. Application of Resource Utilization in Dementia (RUD) instrument in a global setting. *Alzheimers Dement,* 9**,** 429-435 e17.

WIMO, A. & WINBLAD, B. 2003. Societal burden and economics of vascular dementia: preliminary results from a Swedish-population-based study. *Int Psychogeriatr,* 15 Suppl 1**,** 251-6.

WIMO, A., WINBLAD, B. & JONSSON, L. 2010. The worldwide societal costs of dementia: Estimates for 2009. *Alzheimers Dement,* 6**,** 98-103.

WIMO, A., WINBLAD, B., STOFFLER, A., WIRTH, Y. & MOBIUS, H. J. 2003. Resource utilisation and cost analysis of memantine in patients with moderate to severe Alzheimer's disease. *Pharmacoeconomics,* 21**,** 327-40.

WOLFS, C. A. G., DIRKSEN, C. D., KESSELS, A., SEVERENS, J. L. & VERHEY, F. R. J. 2009. Economic evaluation of an integrated diagnostic approach for psychogeriatric patients: results of a randomized controlled trial. *Archives of general psychiatry,* 66**,** 313-23.

WOODS, R., BRUCE, E., EDWARDS, R., ELVISH, R., HOARE, Z., HOUNSOME, B., KEADY, J., MONIZ-COOK, E., ORGETA, V., ORRELL, M., REES, J. & RUSSELL, I. 2012. REMCARE: reminiscence groups for people with dementia and their family caregivers - effectiveness and cost-effectiveness pragmatic multicentre randomised trial. *Health Technology Assessment,* 16**,** 1-121 121p.

YANG, F., DAWES, P., LEROI, I. & GANNON, B. 2017. Measurement tools of resource use and quality of life in clinical trials for dementia or cognitive impairment interventions: protocol for a scoping review. *Systematic Reviews,* 6**,** 22.

Table 1. Characteristics of included studies

Characteristics	**Number (%) of trials, n=41**	
Year of publication		
2000-2005	6	(14.6%)
2006-2010	13	(31.7%)
2011-2017	22	(53.7%)
Country		
United States	12	(29.3%)
United Kingdom	10	(24.4%)
Australia	5	(12.2%)
Finland	2	(4.9%)
Netherlands	2	(4.9%)
Other (1 trial per country) [a]	10	(24.4%)
Type of study		
Pilot study	11	(26.8%)
RCT	30	(73.2%)
Disease		
Mild cognitive impairment only	13	(31.7%)
Dementia only	9	(22.0%)
Both	19	(46.3%)
Intervention		
Pharmacological	5	(12.2%)
Non-pharmacological	35	(85.4%)
Combined	1	(2.4%)

[a] Other countries/regions include Brazil, Denmark, France, Germany, Hong Kong, Japan, Korea, Norway, Sweden and Switzerland.

Table 2. Number (%) of trials reporting QoL outcomes and measurement instruments

	Number (%) of trials, n=41	
Dementia-specific instruments		
Quality of Life in Alzheimer's Disease (QOL-AD)	22	53.7%
Dementia Quality of Life questionnaire (DEMQOL)	4	9.8%
Quality of Life in Late-stage Dementia (QUALID)	3	7.3%
Alzheimer's Disease Related Quality of Life (ADRQL)	2	4.9%
Dementia Quality of Life Instrument (DQOL)	1	2.4%
Generic instruments		
Utility measures		
EuroQol 5-dimentison (EQ-5D)	5	12.2%
15-dimentison (15D)	1	2.4%
Health Utilities Index Mark 3 (HUI3)	1	2.4%
Other measures		
36-item Short-Form (SF-36)	2	4.9%
12-item Short-Form (SF-12)	1	2.4%
12-item General Health Questionnaire (GHQ-12)	1	2.4%
15-item Quality of Life Scales (QOLS)	1	2.4%
Anamnestic Comparative Self-Assessment Scale (ACSA)	1	2.4%
QOL Face Scale scores	1	2.4%
Quality of Life Assessment-Patient (QLA-P)	1	2.4%

Table 3. Characteristics of quality of life instruments used in eligible studies

Instrument	Conceptual basis	Patient report (Yes/No)	Proxy report (Yes/No)	Patient population	Subscales and items	Response options	Scoring
Dementia-specific instruments							
Quality of Life in Alzheimer's Disease (QOL-AD)	Domains validated during focus groups with people with dementia and caregivers	Yes	Yes	Dementia and MCI	13 items for patient version, 15 items for proxy version: physical health; energy level; mood; living situation; memory; family; marriage; friends; self; ability to do chores and things for fun; money; and life as a whole	4-point scales	Score range 13-52 for patient-reported and 15-60 for proxy-rated; high scores represent better QoL
Dementia Quality of Life questionnaire (DEMQOL)	Areas of QoL affected by a health condition	Yes	Yes	Dementia and MCI	5 domains (28 items for patient, 31 items for proxy): daily activities and looking after self; health and well-being; cognitive functioning; social relationships; self-concept	4-point Likert scales	Score range 28-112 for DEMQOL and 31-124 for DEMQOL-Proxy; high scores indicate better QoL
Quality of Life in Late-stage Dementia (QUALID)	Affect and activity measures for use with late-stage dementia patients	No	Yes	Severe dementia	11 observable behaviours of observable activity and emotional states	5-point Likert scales	Score range 11-55; lower scores represent better QoL
Alzheimer's Disease Related Quality of Life (ADRQL)	Domains of QoL that their caregivers and experts identified as important	No	Yes	Dementia and MCI	5 domains (48 items): social interaction; awareness of self; feelings and mood; enjoyment of activities; response to surroundings	4-point Likert scales	Score calculated using a preference-based weighting approach; higher scores represent better QoL
Dementia Quality of Life Instrument (DQOL)	Feeling states and mood	Yes	No	Dementia and MCI	5 subscales (30 items): aesthetics; positive affect; absence of negative affect; belonging; and self-esteem	5-point Likert scales	Scores on 5 subscales without overall score; lower scores on negative affect and higher scores on the other subscales indicate better QoL
Generic instruments							
EuroQol 5-dimentison (EQ-5D)	Health defined using a descriptive system in domains and levels for each domain	Yes	Yes	Dementia and MCI	5 domains: mobility; self-care; usual activities; pain/discomfort; and anxiety/depression	3-level for each domain	Scores calculated using social weights; range from -0.594-1 (UK weights); higher scores reflects better health

15-dimentison (15D)	Health defined using a descriptive system in 15 dimensions	Yes	No	MCI	15 dimensions: mobility; vision; hearing; breathing; sleeping; eating; speech; excretion; usual activities; mental function; discomfort and symptoms; depression; distress; vitality; and sexual activity	5 levels for each dimensions	Scores calculated using social weights; range 0-1; higher scores reflects better health
Health Utilities Index Mark 3 (HUI3)	Health defined using a descriptive system in attributes and levels within each attribute	No	Yes	Dementia and MCI	8 attributes: hearing; vision; speech; ambulation; dexterity; emotion; cognition; and pain	3-6 functional levels for each attribute	Score range -0.36-1; higher scores reflects better health
36-item Short-Form (SF-36) and 12-item Short-Form (SF-12)	Health concepts that are relevant to patients from patient's perspective	Yes	No	MCI	8 areas: physical functioning; role functioning; bodily pain; general health; vitality; social functioning; role-emotional functioning; and mental health	2-6 levels for each question	Summary scores, PCS and MCS, range from 0-100; higher scores reflects better health
12-item General Health Questionnaire (GHQ-12)	Psychiatric disorder	Yes	No	Dementia and MCI	2 main areas (12 items): the inability to carry out normal functions; the appearance of new and distressing phenomena	4-point scale	Score range 0-36, lower indicate better health
15-item Quality of Life Scales (QOLS)	Items derived from a general public sample by researchers	Yes	No	MCI	5 domains (15 items): material and physical well-being; relationships with other people; social, community, and civic activities; personal development and fulfilment; and recreation	7-point scale	Score range 16-112; higher scores reflects better health
Anamnestic Comparative Self-Assessment Scale (ACSA)	Subjective well-being defined in terms of the 'best time' versus the 'worst time' in life	Yes	No	MCI	/	10-stage anchor scale	An improvement in global scale score reflects higher quality of life
QOL Face Scale	Degree of general happiness in current daily life	No	Yes	MCI	/	9-choice picture format	Score range 1-9; higher scores indicate better QoL
Quality of Life Assessment-Patient (QLA-P)	Broad areas of patient's quality of life	No	Yes	Dementia	10 categories: working; leisure; eating; sleeping; social contact; earning; parenting; loving; environment; and self-acceptance	Anchor-point	Scale range 0-50; higher scores indicate better QoL

*MCI: mild cognitive impairment

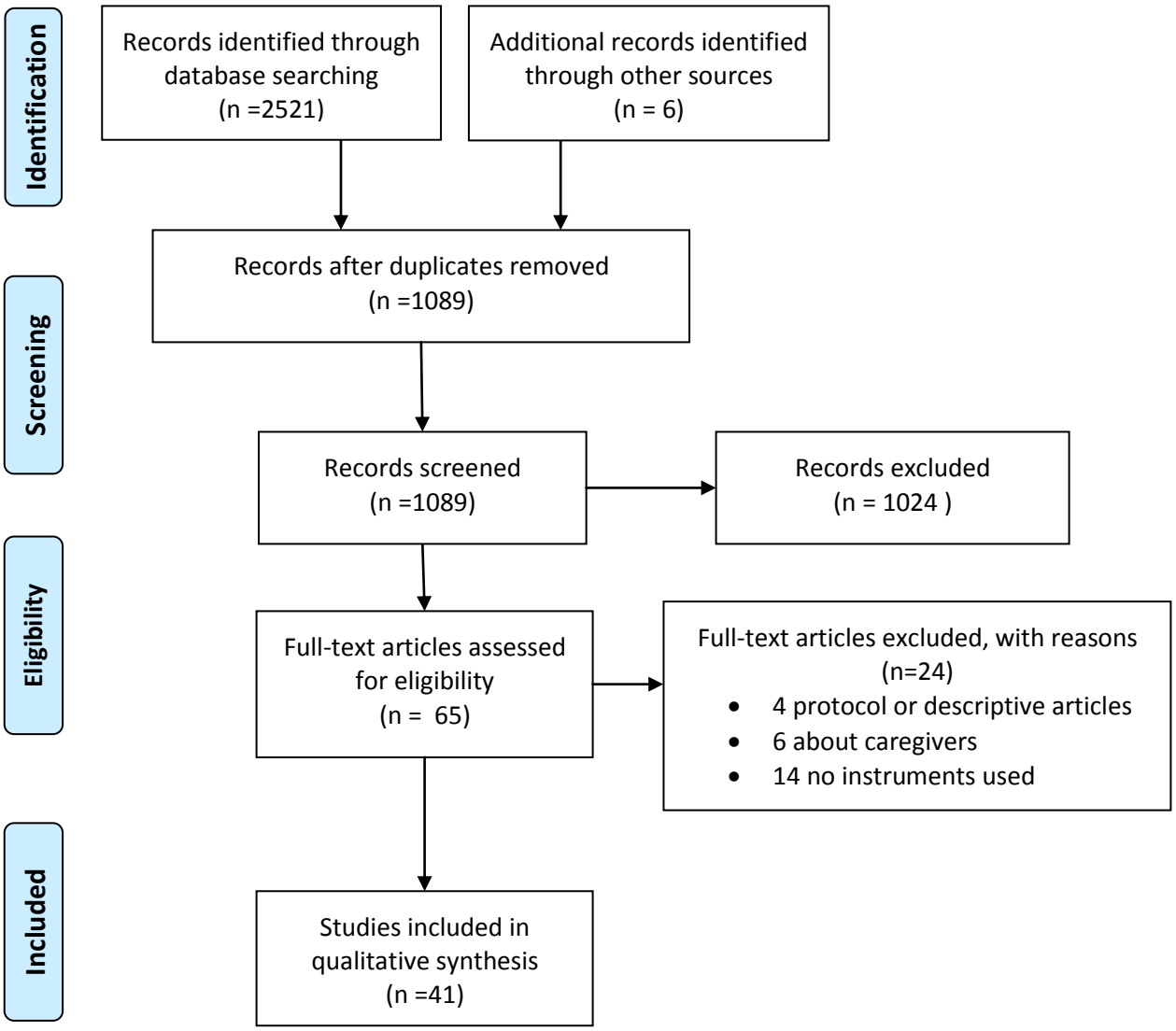

Figure 1. PRISMA flow diagram identification, screening, eligibility and included articles.

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Appendix S1. Search terms for Ovid Medline

1	exp dementia/ or exp alzheimer disease/ or exp cognitive impairment/
2	sensory impairment.ti,ab.
3	1 or 2
4	exp aged/ or exp frail elderly/
5	(older or old or elderly or senior or "over 65" or "65 year*").ti,ab.
6	4 or 5
7	Economics, Medical/ or Economics/ or Economics, Hospital/ or Economics, Nursing/
8	exp "Costs and Cost Analysis"/
9	Health Expenditures/
10	("resource use" or "health care utilisation" or "health care utilization" or "resource utilisation" or "resource utilization").ti,ab.
11	7 or 8 or 9 or 10
12	"Quality of Life"/
13	Quality-Adjusted Life Years/
14	("health utility" or QALY).ti,ab.
15	12 or 13 or 14
16	11 or 15
17	(intervention or program or promotion).ti,ab.
18	Clinical Trial/
19	Feasibility Studies/
20	Pilot Projects/
21	(trial or feasibility or pilot).ti,ab.
22	18 or 19 or 20 or 21
23	3 and 6 and 16 and 17 and 22